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Giant-cell myocarditis management using short-term TandemHeart support, MANTA closure device, and combination immunosuppression

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ABSTRACT

We present the case of a 53-year-old woman who presented to the hospital with palpitations and fatigue. The workup revealed new-onset systolic heart failure secondary to giant cell myocarditis. She developed cardiogenic shock, which was managed with the TandemHeart left ventricular assist device and combination immunosuppression strategy. This article highlights our management approach that avoided the need for an urgent heart transplant.

KEYWORDS Acute heart failure; autoimmune disease; mechanical circulatory support; myocarditis; ventricular tachycardia

Giant cell myocarditis (GCM) is an extremely rare and aggressive T lymphocyte–mediated autoimmune disease with high cardiovascular morbidity and mortality, especially if not diagnosed early in the disease course.[1] There is scant evidence regarding the best management approach for patients with GCM, especially the best immunosuppression strategy. We present our diagnostic and management approach for a unique patient.

CASE DESCRIPTION

A 53-year-old white woman presented to an outside hospital with fatigue and palpitations for 2 weeks. Diagnostic workup revealed a reduced left ventricular ejection fraction (LVEF) on transthoracic echocardiogram, a normal coronary angiogram, and premature ventricular contractions (PVCs) on telemetry. She was discharged home with a Holter monitor, but 1 week later, she was readmitted when the monitor revealed a high burden of PVCs and nonsustained ventricular tachycardia. During this admission, her ejection fraction was 10%. She was transferred to our center for further management. Upon arrival, she was asymptomatic and hemodynamically stable, with elevated brain natriuretic protein and troponin levels, but normal renal and liver function. Numerous multifocal PVCs were noted on electrocardiogram and telemetry. She had a history of well-controlled serology-positive systemic lupus erythematosus diagnosed 20 years earlier and had been on hydroxychloroquine for more than 10 years. Her body mass index was 38.8 kg/m^2.

Cardiac magnetic resonance imaging revealed late gadolinium enhancement in both ventricles involving multiple patchy areas with relative preservation of the lateral wall *(Figure 1)*. The LVEF was 18%, and the right ventricular ejection fraction was 24%. Endomyocardial biopsy on admission was consistent with GCM *(Figure 2a, 2b)*. The large majority of lymphocytes were T cells (CD4, CD8) with only rare CD20 B lymphocytes. CD68 showed giant cells were of macrophage origin.

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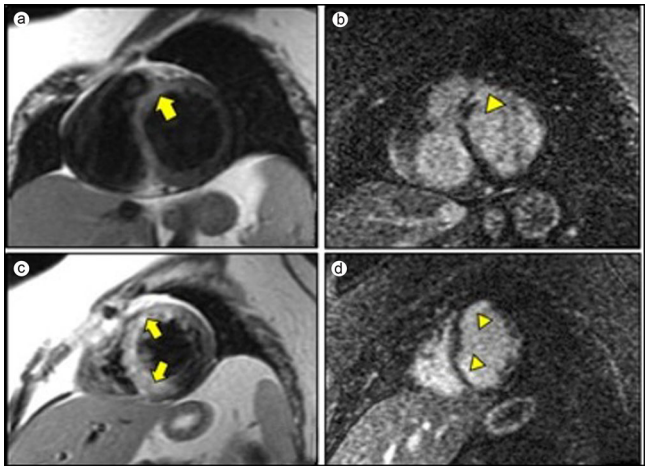

Figure 1. Cardiac magnetic resonance imaging. **(a, b)** Short axis images through the heart showing patchy edema on T2 images (arrows), **(c, d)** with corresponding areas of patchy mid-myocardial and sub-endocardial late gadolinium enhancement (arrowheads).

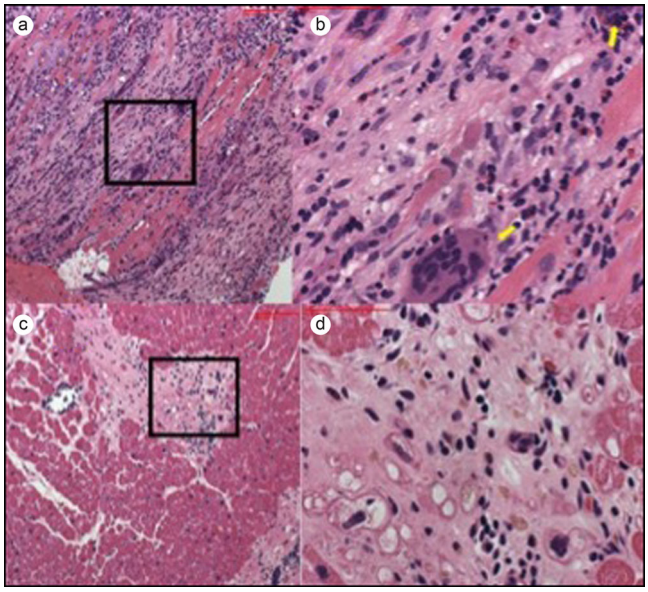

Figure 2. Histology. **(a)** 10× and **(b)** 40× showing a prominent polymorphous inflammatory infiltrate composed of lymphocytes, macrophages, numerous eosinophils, and giant cells (yellow arrow) in a background of myocyte damage. **(c)** 10× and **(d)** 40× showing areas of healing injury with granulation tissue and hemosiderin-laden macrophages. No active inflammation is seen.

The patient was started on immunosuppression with methylprednisolone, tacrolimus, and mycophenolate. She could not tolerate metoprolol tartrate 12.5 mg due to symptomatic hypotension. By day 3, PVCs and nonsustained ventricular tachycardia persisted despite amiodarone and lidocaine infusion. She also developed acute kidney injury with a serum creatinine of 2 mg/dL. Right heart catheterization showed elevated pulmonary capillary wedge pressure at 37 mm Hg and a depressed Fick cardiac index of 1.93 L/min.

At this stage, a TandemHeart mechanical circulatory support device was placed, significantly reducing ventricular ectopy. An esmolol infusion led to near-complete resolution of arrhythmias, with a resting heart rate of 60 bpm. The TandemHeart was removed after 10 days. Her pulmonary capillary wedge pressure improved to 17 mm Hg, and her cardiac index was 2.7 L/min. Her LVEF was 35% at the time of removal. Empiric antibiotics were initiated during TandemHeart support and discontinued following removal.

The MANTA, a novel collagen-based large-bore vessel closure device, was used for arterial closure after decannulation *(Figure 3)*. After successful removal of the TandemHeart, there was recurrence of PVCs and rare nonsustained ventricular tachycardia, which were believed to be due in part to a lower goal tacrolimus level of 6 to 8 ng/mL due to acute kidney injury. Again, ventricular ectopy responded well to additional pulse-dose steroids and resumption of esmolol infusion, which she tolerated well this time. Nineteen days after diagnosis, a repeat biopsy demonstrated resolution of inflammation *(Figure 2c, 2d)*.

On day 26 of treatment, a repeat transthoracic echocardiogram showed continued improvement in LVEF to 35% to 40%. An esmolol drip was transitioned to metoprolol tartrate 75 mg three times a day. After implantable cardioverter defibrillator implant, she was discharged on a slow prednisone taper, tacrolimus 2.5 mg twice a day, and mycophenolic acid 720 mg twice a day. Unfortunately, a week after discharge, she was readmitted with a bilateral groin infection requiring surgical exploration and antibiotic bead placement. She then underwent right femoral thrombectomy with the removal of the MANTA footplate and wound-vac placement.

DISCUSSION

To the best of our knowledge, this is the first reported case using TandemHeart in the management of GCM-related cardiogenic shock. TandemHeart was chosen for our patient as the least invasive mode of mechanical circulatory support with the goal of transplant- and device-free myocardial recovery.[2] Less hemolysis is associated with TandemHeart and, thus, less related renal injury, which is particularly important in the setting of nephrotoxic immunosuppressants. In the acute phase of the disease, mechanical circulatory support mitigates the immediate threat of fatal ventricular arrhythmia in GCM and associated cardiogenic shock by ensuring adequate tissue perfusion and obviating the need for inotropes.[3] It promotes myocardial recovery in parallel with immunosuppression by rapid volume unloading.[4]

The combination of TandemHeart (flow 2.8 LPM and speed 5800 RPM) and nitroglycerin infusion decreased our patient's filling pressures to normal. Nitroglycerin was weaned within 36 hours. Early weaning trials of TandemHeart guided by bedside echocardiogram and filling pressures as measured by pulmonary artery catheter were unsuccessful: Reducing flow led to significant dilation of the

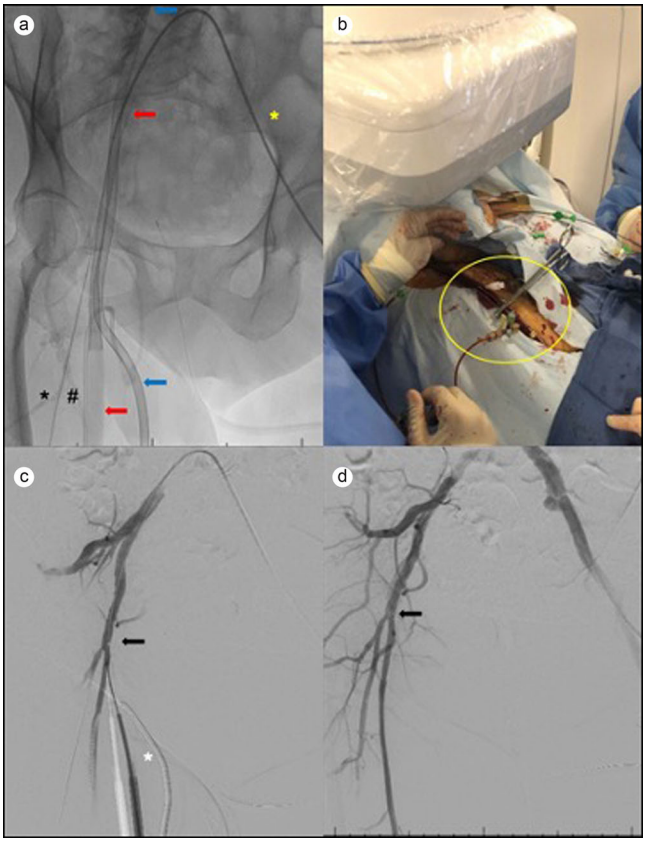

Figure 3. MANTA vessel closure device. **(a)** Initial retrograde access across the right common femoral artery. The 6F 45-cm Terumo destination sheath (yellow asterisk) was inserted with the tip positioned in the right common iliac artery, over an 0.035-inch wire (black asterisk), which was positioned in the right profunda femoris. The 21F left atrial cannula is seen originating from the right femoral vein (blue arrow). The 17F arterial cannula is seen in the right common femoral artery (red arrow). A 6F distal perfusion sheath is seen in the right superficial femoral artery (black pound symbol). **(b)** A micropuncture sheath was used to gain wire access to the arterial cannula. **(c)** Angiography after deployment of MANTA. The delivery tube (white asterisk) and radiopaque marker (black arrow) are seen. **(d)** Final angiography after full MANTA closure and Mynx closure of the distal perfusion sheath.

right ventricle along with an increase in filling pressures. After 10 days of support, our patient's ejection fraction had improved to 35%. She was euvolemic with stable renal function and stable filling pressures despite decreasing support. Ectopy had resolved, and her resting heart rate was 60 to 70 bpm with esmolol infusion. TandemHeart was successfully removed.

The large-bore vessel closure device MANTA worked well in our case to prevent major bleeding complications during and immediately following decannulation.[5] Unfortunately, she developed bilateral groin infections prompting readmission. Since acute GCM is treated with heavy immunosuppression, which leads to impaired wound healing and increased risk of infection, we speculate that it would have been prudent to extend empiric antibiotics until adequate healing had occurred at large-bore vascular access sites.

There is no established guideline for immunosuppressive therapy for GCM; however, combination therapy including various combinations of prednisone, calcineurin inhibitors (tacrolimus or cyclosporine), and antimetabolites (azathioprine and mycophenolate) has been reported to reverse cardiogenic shock into mild systolic heart failure.[2] Our immunosuppression strategy was akin to post-heart transplantation. However, we chose a lower tacrolimus trough goal of 6 to 8 ng/mL for renal protection.[6] The fact that repeat biopsy showed resolution of inflammation indicates that this trough level provides adequate immunosuppression, but this may vary by patient.

In conclusion, TandemHeart and immunosuppression therapy with prednisone, tacrolimus, and mycophenolate in the acute phase of GCM were the keys to successful transplant- and device-free recovery.

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